| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 1 | BRS | L1 | 434 | melanocyte-stimulating adj hormone | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:07 | | | 0 |
| 2 | BRS | L2 | 151 | inhibit$3 same 1 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:08 | | | 0 |
| 3 | BRS | L3 | 3973 | cAMP same produc$5 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:08 | | | 0 |
| 4 | BRS | L5 | 10296 | IC50 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:09 | | | 0 |
| 5 | BRS | L4 | 3 | 2 same 3 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:09 | | | 0 |
| 6 | BRS | L6 | 2 | 4 same 5 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:12 | | | 0 |
| 7 | BRS | L7 | 2 | pigment$5 same ultrviolet | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:12 | | | 0 |
| 8 | BRS | L8 | 0 | 7 same 4 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:13 | | | 0 |
| 9 | BRS | L9 | 0 | (molecular adj weight) same 4 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:14 | | | 0 |
| 10 | BRS | L10 | 6092 | whitening adj agent | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:15 | | | 0 |
| 11 | BRS | L11 | 11 | immuno$7 adj controlling adj agent | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:16 | | | 0 |
| 12 | BRS | L12 | 7 | appetite adj controlling adj agent | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:16 | | | 0 |
| 13 | BRS | L13 | 20110 | cosmetic adj (composition or preparation) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:17 | | | 0 |
| 14 | BRS | L14 | 1 | (10 or 11 or 12 or 13) same 2 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:20 | | | 0 |
| 15 | BRS | L15 | 2 | wo-9512611-$.did. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:19 | | | 0 |
| 16 | BRS | L16 | 0 | (10 or 11 or 12 or 13) same 4 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:20 | | | 0 |

| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 17 | BRS | L17 | 16 | shiojiri adj eiji.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:21 | | | 0 |
| 18 | BRS | L18 | 34 | takino adj yoshinobu.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:21 | | | 0 |
| 19 | BRS | L19 | 1 | chujou adj hiromi.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:22 | | | 0 |
| 20 | BRS | L20 | 16 | sakamoto adj kazutami.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:22 | | | 0 |
| 21 | BRS | L21 | 0 | ljichi adj chiori.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:23 | | | 0 |
| 22 | BRS | L22 | 52 | eto adj yuzuru.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:23 | | | 0 |
| 23 | BRS | L23 | 67 | iwasaki adj keiji.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:24 | | | 0 |
| 24 | BRS | L24 | 1 | (17 or 18 or 19 or 20 or 22) and l2 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:24 | | | 0 |

| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 1 | BRS | L1 | 434 | melanocyte-stimulating adj hormone | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:26 | | | 0 |
| 2 | BRS | L2 | 151 | inhibit$3 same (melanocyte-stimulating adj hormone) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:26 | | | 0 |
| 3 | BRS | L3 | 134 | naphthyl same (dipeptide or tripeptide) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:27 | | | 0 |
| 4 | BRS | L4 | 1 | 2 same 3 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/09/16 19:27 | | | 0 |

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FILE 'MEDLINE' ENTERED AT 19:32:01 ON 16 SEP 2003

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FILE 'SCISEARCH' ENTERED AT 19:32:01 ON 16 SEP 2003
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FILE 'AGRICOLA' ENTERED AT 19:32:01 ON 16 SEP 2003

=> s melanocyte stimulating hormone
L1       11488 MELANOCYTE STIMULATING HORMONE

=> s l1 (p) Inhibit?
L2        2488 L1 (P) INHIBIT?

=> s naphthyl (p) (dipeptide or tripeptide)
L3         224 NAPHTHYL (P) (DIPEPTIDE OR TRIPEPTIDE)

=> s l3 (p) l2
L4           0 L3 (P) L2

=> s cAMP (p) produc?
L5       69265 CAMP (P) PRODUC?

=> s l2 (p) l5
L6          71 L2 (P) L5

=> s IC50
L7      122666 IC50

=> s l7 (p) l6
L8           0 L7 (P) L6

=> s l6 (p) (50%) (p) inhibit?
L9           6 L6 (P) (50%) (P) INHIBIT?

=> duplicate remove l9
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L9
L10           2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)

=> d l10 1-2 ibib abs

L10  ANSWER 1 OF 2     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2001486152     MEDLINE
DOCUMENT NUMBER:     21419775   PubMed ID: 11528221
TITLE:               Expression of functional melanocortin-4 receptor in the
                     hypothalamic GT1-1 cell line.
AUTHOR:              Khong K; Kurtz S E; Sykes R L; Cone R D
CORPORATE SOURCE:    Vollum Institute, Oregon Health Sciences University,
                     Portland, Oreg. 97201, USA.
CONTRACT NUMBER:     DK51730 (NIDDK)
SOURCE:              NEUROENDOCRINOLOGY, (2001 Sep) 74 (3) 193-201.
                     Journal code: 0035665. ISSN: 0028-3835.
PUB. COUNTRY:        Switzerland
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200112
ENTRY DATE:          Entered STN: 20010903
                     Last Updated on STN: 20020122
                     Entered Medline: 20011204
AB   Mutations in the melanocortin-4 receptor (MC4-R) cause obesity in both
     mice and humans, and the receptor is presumed to have an important role in
     the regulation of energy homeostasis.  The MC4-R is expressed in discrete
     sets of neurons in the central nervous system, and thus it has been
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technically difficult to study the regulation of expression and the signaling mechanisms of this receptor. We report here a neuronal cell line that exhibits endogenous functional expression for the MC4-R. Initially, RT-PCR analysis showed the presence of MC4-R RNA in the hypothalamic GT1-1 and GT1-7 cells. In addition, GT1-7 cells expressed melanocortin-3 receptor while the GT1-1 subclone specifically expressed predominantly the MC4-R RNA. High-affinity binding sites were demonstrated in the GT1-1 and GT1-7 cells for NDP-alpha ***melanocyte*** - ***stimulating*** ***hormone*** (MSH; K(i) = 1.1 x 10(-10) and 1.8 x 10(-10) M) and agouti-related protein (AGRP; K(i) = 1.548 x 10(-9) and 1.663(-9) M). alpha-MSH-stimulated ***cAMP*** ***production*** in GT1-1 cells with an EC( ***50*** ) of 2.2 x 10(-8) M, and ***cAMP*** ***production*** was ***inhibited*** in the presence of AGRP, an endogenous antagonist of the MC4-R. Stimulation of gonadotropin-releasing hormone (GnRH) secretion was achieved with 1 nM to 1 microM concentrations of NDP-alpha-MSH while no GnRH secretion was observed when the GT1-1 cells were treated with AGRP. The data presented here show that GT1-1 cells specifically express a functional MC4-R that couples to GnRH release.



L10 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 97021894 MEDLINE
DOCUMENT NUMBER: 97021894 PubMed ID: 8868254
TITLE: Adenosine inhibits L- and N-type calcium channels in pituitary melanotrophs. Evidence for the involvement of a G protein in calcium channel gating.
AUTHOR: Mei Y A; Le Foll F; Vaudry H; Cazin L
CORPORATE SOURCE: Laboratory of Cellular and Molecular Neuroendocrinology, INSERM U 413, University of Rouen, Mont-Saint-Aignan, France.
SOURCE: JOURNAL OF NEUROENDOCRINOLOGY, (1996 Feb) 8 (2) 85-91. Journal code: 8913461. ISSN: 0953-8194.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 20021218
Entered Medline: 19961127

AB It has been previously demonstrated that activation of A1 adenosine receptors in frog melanotrophs causes ***inhibition*** of spontaneous action potential discharges and alpha- ***melanocyte*** - ***stimulating*** ***hormone*** secretion. In the present study, we have investigated the effect of adenosine on high-voltage-activated (HVA) calcium currents in cultured melanotrophs, using the whole-cell variant of the patch-clamp technique with barium as a charge carrier. Adenosine and the specific A1 adenosine receptor agonist R-PIA ( ***50*** microM each) ***produced*** a decrease of the amplitude of the barium current, while the selective A2 adenosine receptor agonist CGS 21680 did not affect the current. The ***inhibitory*** effect of R-PIA was observed throughout the activation range of the current, with stronger responses at more positive potentials. R-PIA ***inhibited*** both the L- and N-type components of the current, the effect on the N-component being two-fold higher than on the L-component. The ***inhibitory*** effect of R-PIA was rendered irreversible by addition of GTP gamma S (100 microM) to the intracellular solution. Pre-treatment of the cells with pertussis toxin (1 microgram/ml; 12 h) totally abolished the effect of R-PIA on the HVA calcium channels. Conversely, addition of a high concentration of ***cAMP*** (100 microM) together with the phosphodiesterase ***inhibitor*** IBMX (100 microM) to the intracellular solution did not modify the effect of R-PIA on the current. It is concluded that, in frog melanotrophs, adenosine induces ***inhibition*** of L- and N-calcium currents and that this effect is mediated by a pertussis toxin-sensitive G protein. Our data also indicate that the ***inhibitory*** effect of adenosine on the calcium currents is not mediated by ***inhibition*** of adenylyl cyclase.

=> d his

(FILE 'HOME' ENTERED AT 19:31:37 ON 16 SEP 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 19:32:01 ON 16 SEP 2003
L1 11488 S MELANOCYTE STIMULATING HORMONE

```
L2          2488 S L1 (P) INHIBIT?
L3           224 S NAPHTHYL (P) (DIPEPTIDE OR TRIPEPTIDE)
L4             0 S L3 (P) L2
L5         69265 S CAMP (P) PRODUC?
L6            71 S L2 (P) L5
L7        122666 S IC50
L8             0 S L7 (P) L6
L9             6 S L6 (P) (50%) (P) INHIBIT?
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)

=> duplicate remove l6
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L6
L11           25 DUPLICATE REMOVE L6 (46 DUPLICATES REMOVED)

=> d l11 1-25 ibib abs

L11  ANSWER 1 OF 25     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2001163129     MEDLINE
DOCUMENT NUMBER:     21134400   PubMed ID: 11239505
TITLE:               Effects of melanocortin peptides on
                     lipopolysaccharide/interferon-gamma-induced NF-kappaB DNA
                     binding and nitric oxide production in macrophage-like RAW
                     264.7 cells: evidence for dual mechanisms of action.
AUTHOR:              Mandrika I; Muceniece R; Wikberg J E
CORPORATE SOURCE:    Department of Pharmaceutical Pharmacology, Uppsala
                     University, Box 591, BMC, SE-75124, Uppsala, Sweden.
SOURCE:              BIOCHEMICAL PHARMACOLOGY, (2001 Mar 1) 61 (5) 613-21.
                     Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY:        England: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200104
ENTRY DATE:          Entered STN: 20010410
                     Last Updated on STN: 20010410
                     Entered Medline: 20010405
AB   The pro-opiomelanocortin-derived peptide alpha-  ***melanocyte***  -
       ***stimulating***     ***hormone***   (alpha-MSH) mediates broad
     anti-inflammatory and immunomodulatory effects, which include
       ***inhibition***   of the   ***production***   and release of
     proinflammatory cytokines and nitric oxide (NO) from macrophages.  We
     investigated the effects of alpha-MSH, alpha-MSH(1-10), and
     alpha-MSH(11-13) on NO   ***production***   and nuclear factor-kappaB
     (NF-kappaB) translocation in RAW 264.7 macrophages.  After stimulation of
     the cells with bacterial lipopolysaccharide/interferon-gamma
     (LPS/IFN-gamma), all three peptides   ***inhibited***   NO
       ***production***   with an order of potency alpha-MSH > or =
     alpha-MSH(11-13) > alpha-MSH(1-10).  All three MSH peptides
       ***inhibited***   NF-kappaB nuclear translocation with the maximal effect
     of alpha-MSH and alpha-MSH(11-13) being seen in the range 1 nM-1 microM,
     and that of alpha-MSH(1-10) at 1 microM.  By use of (125)I-(Nle(4),D-
     Phe(7))alpha-MSH(NDP-MSH) radioligand binding, MC(1) receptor-binding
     sites were demonstrated on RAW 264.7 cells. alpha-MSH and alpha-MSH(1-10)
     competed with the (125)I-NDP-MSH binding at these MC(1) receptor-binding
     sites, but alpha-MSH(11-13) even in concentrations up to 1 mM did not.
     Moreover, alpha-MSH and alpha-MSH(1-10) caused powerful stimulation of
     cyclic 3',5'-adenosine monophosphate (  ***cAMP***  ) in the RAW 264.7
     cell, whereas alpha-MSH(11-13) was ineffective.  Forskolin stimulated
       ***cAMP***   and   ***inhibited***   NO   ***production***   to the same
     extent as alpha-MSH and alpha-MSH(1-10), but did not modify the
     translocation of NF-kappaB.  Whereas the protein kinase A
       ***inhibitor***   H89 did not modify the effect of alpha-MSH on NF-kappaB
     translocation, H89 caused a partial   ***inhibition***   of the
       ***inhibitory***   effect of alpha-MSH, alpha-MSH(1-10), alpha-MSH(11-13),
     and forskolin on NO   ***production***   .  In addition alpha-MSH,
     alpha-MSH(1-10), alpha-MSH(11-13), and forskolin also   ***inhibited***
     the activity of an NF-kappaB-dependent luciferase reporter and these
     effects were partially counteracted by H89.  We suggest that melanocortin
     peptides act via dual mechanisms of action: one   ***cAMP***  -independent
     and causing   ***inhibition***   of NF-kappaB translocation and the other
     dependent on MC(1) receptor/  ***cAMP***   activation.

L11  ANSWER 2 OF 25     MEDLINE on STN                    DUPLICATE 2
ACCESSION NUMBER:    2001486152     MEDLINE
DOCUMENT NUMBER:     21419775   PubMed ID: 11528221
```

TITLE: Expression of functional melanocortin-4 receptor in the hypothalamic GT1-1 cell line.
AUTHOR: Khong K; Kurtz S E; Sykes R L; Cone R D
CORPORATE SOURCE: Vollum Institute, Oregon Health Sciences University, Portland, Oreg. 97201, USA.
CONTRACT NUMBER: DK51730 (NIDDK)
SOURCE: NEUROENDOCRINOLOGY, (2001 Sep) 74 (3) 193-201.
Journal code: 0035665. ISSN: 0028-3835.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20020122
Entered Medline: 20011204

AB Mutations in the melanocortin-4 receptor (MC4-R) cause obesity in both mice and humans, and the receptor is presumed to have an important role in the regulation of energy homeostasis. The MC4-R is expressed in discrete sets of neurons in the central nervous system, and thus it has been technically difficult to study the regulation of expression and the signaling mechanisms of this receptor. We report here a neuronal cell line that exhibits endogenous functional expression for the MC4-R. Initially, RT-PCR analysis showed the presence of MC4-R RNA in the hypothalamic GT1-1 and GT1-7 cells. In addition, GT1-7 cells expressed melanocortin-3 receptor while the GT1-1 subclone specifically expressed predominantly the MC4-R RNA. High-affinity binding sites were demonstrated in the GT1-1 and GT1-7 cells for NDP-alpha ***melanocyte*** - ***stimulating*** ***hormone*** (MSH; K(i) = 1.1 x 10(-10) and 1.8 x 10(-10) M) and agouti-related protein (AGRP; K(i) = 1.548 x 10(-9) and 1.663(-9) M). alpha-MSH-stimulated ***cAMP*** ***production*** in GT1-1 cells with an EC(50) of 2.2 x 10(-8) M, and ***cAMP*** ***production*** was ***inhibited*** in the presence of AGRP, an endogenous antagonist of the MC4-R. Stimulation of gonadotropin-releasing hormone (GnRH) secretion was achieved with 1 nM to 1 microM concentrations of NDP-alpha-MSH while no GnRH secretion was observed when the GT1-1 cells were treated with AGRP. The data presented here show that GT1-1 cells specifically express a functional MC4-R that couples to GnRH release.


L11 ANSWER 3 OF 25 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1998421778 MEDLINE
DOCUMENT NUMBER: 98421778 PubMed ID: 9751158
TITLE: Melanocortin receptors and delta-opioid receptor mediate opposite signalling actions of POMC-derived peptides in CATH.a cells.
AUTHOR: Rene F; Muller A; Jover E; Kieffer B; Koch B; Loeffler J P
CORPORATE SOURCE: Laboratoire de Neurophysiologie Cellulaire et Integree, UMR CNRS 7519, Strasbourg, France.
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (1998 May) 10 (5) 1885-94.
Journal code: 8918110. ISSN: 0953-816X.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981022

AB The locus coeruleus is innervated by proopiomelanocortin (POMC)-derived peptide immunoreactive fibres. The biological effects of ( ***melanocyte*** - ***stimulating*** ***hormone*** (aMSH) and [-endorphin on second messengers ( ***cAMP*** , inositol phosphates) and gene transcription were studied in the locus cceruleus-derived cell line CATH.a. RT-PCR analysis revealed the presence of four MSH receptor subtypes (1, 3, 4 and 5). Activation of these receptors by diacetyl alphaMSH stimulated ***cAMP*** accumulation in a dose-dependent manner (EC50: 4 x 10(-9) M). Diacetyl alphaMSH stimulated transcription from reporter genes driven by the c-fos or tyrosine hydroxylase promoter. This effect was abolished when protein kinase A was inactivated with a dominant ***inhibitory*** mutant. RT-PCR analyses revealed the presence of delta-, but not mu-and kappa-opioid receptor. Pharmacological analysis showed that beta-endorphin (EC50: 2.5 x 10(-8)M), but not N-acetyl beta-endorphin, antagonized the biological effect of diacetyl alphaMSH on ***cAMP*** ***production*** and gene transcription. Since N-acetylation regulates the biological activity of alphaMSH and

beta-endorphin in an opposite manner, we propose a model where the rate of secretion dictated by the bioelectric activity of the presynaptic neuron modulates POMC-derived peptide maturation and the resulting biological signal sensed by the postsynaptic plate.

L11 ANSWER 4 OF 25 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1998281989 MEDLINE
DOCUMENT NUMBER: 98281989 PubMed ID: 9620667
TITLE: Melanocortin peptides inhibit production of proinflammatory cytokines and nitric oxide by activated microglia.
AUTHOR: Delgado R; Carlin A; Airaghi L; Demitri M T; Meda L; Galimberti D; Baron P; Lipton J M; Catania A
CORPORATE SOURCE: III Division of Internal Medicine, IRCCS Ospedale Maggiore, Milano, Italy.
CONTRACT NUMBER: NS10046 (NINDS)
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1998 Jun) 63 (6) 740-5.
Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625

AB Inflammatory processes contribute to neurodegenerative disease, stroke, encephalitis, and other central nervous system (CNS) disorders. Activated microglia are a source of cytokines and other inflammatory agents within the CNS and it is therefore important to control glial function in order to preserve neural cells. Melanocortin peptides are pro-opiomelanocortin-derived amino acid sequences that include alpha- ***melanocyte*** - ***stimulating*** ***hormone*** (alpha-MSH) and adrenocorticotropic hormone (ACTH). These peptides have potent and broad anti-inflammatory effects. We tested effects of alpha-MSH (1-13), alpha-MSH (11-13), and ACTH (1-24) on ***production*** of tumor necrosis factor alpha (TNF-alpha), interleukin-6 (IL-6), and nitric oxide (NO) in a cultured murine microglial cell line (N9) stimulated with lipopolysaccharide (LPS) plus interferon gamma (IFN-gamma). Melanocortin peptides ***inhibited*** ***production*** of these cytokines and NO in a concentration-related fashion, probably by increasing intracellular ***cAMP*** . When stimulated with LPS + IFN-gamma, microglia increased release of alpha-MSH. ***Production*** of TNF-alpha, IL-6, and NO was greater in activated microglia after innmunoneutralization of endogenous alpha-MSH. The results suggest that alpha-MSH is an autocrine factor in microglia. Because melanocortin peptides ***inhibit*** ***production*** of pro-inflammatory mediators by activated microglia they might be useful in treatment of inflammatory/degenerative brain disorders.

L11 ANSWER 5 OF 25 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 97325795 MEDLINE
DOCUMENT NUMBER: 97325795 PubMed ID: 9182807
TITLE: Agouti signaling protein inhibits melanogenesis and the response of human melanocytes to alpha-melanotropin.
AUTHOR: Suzuki I; Tada A; Ollmann M M; Barsh G S; Im S; Lamoreux M L; Hearing V J; Nordlund J J; Abdel-Malek Z A
CORPORATE SOURCE: POLA Laboratories, Yokohama, Japan.
CONTRACT NUMBER: EY 10223 (NEI)
R01 ES06882-01 A1 (NIEHS)
SOURCE: JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1997 Jun) 108 (6) 838-42.
Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970716
Last Updated on STN: 19970716
Entered Medline: 19970630

AB In mouse follicular melanocytes, the switch between eumelanin and pheomelanin synthesis is regulated by the extension locus, which encodes the melanocortin-1 receptor (MC1R) and the agouti locus, which encodes a novel paracrine-signaling molecule that ***inhibits*** binding of melanocortins to the MC1R. Human melanocytes express the MC1R and respond to melanotropins with increased proliferation and eumelanogenesis, but a potential role for the human homolog of agouti-signaling protein, ASIP, in

human pigmentation has not been investigated. Here we report that ASIP blocked the binding of alpha- ***melanocyte*** - ***stimulating*** ***hormone*** (alpha-MSH) to the MC1R and ***inhibited*** the effects of alpha-MSH on human melanocytes. Treatment of human melanocytes with 1 nM-10 nM recombinant mouse or human ASIP blocked the stimulatory effects of alpha-MSH on ***cAMP*** accumulation, tyrosinase activity, and cell proliferation. In the absence of exogenous alpha-MSH, ASIP ***inhibited*** basal levels of tyrosinase activity and cell proliferation and reduced the level of immunoreactive tyrosinase-related protein-1 (TRP-1) without significantly altering the level of immunoreactive tyrosinase. In addition, ASIP blocked the stimulatory effects of forskolin or dibutyryl ***cAMP*** , agents that act downstream from the MC1R, on tyrosinase activity and cell proliferation. These results demonstrate that the functional relationship between the agouti and MC1R gene ***products*** is similar in mice and humans and suggest a potential physiologic role for ASIP in regulation of human pigmentation.

L11 ANSWER 6 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 6
ACCESSION NUMBER: 1998:95652 BIOSIS
DOCUMENT NUMBER: PREV199800095652
TITLE: Expression of signal transducing G proteins in human melanoma cell lines.
AUTHOR(S): Lee, Eun-So; Kang, Won Hyoung; Jin, Yoon-Hi; Juhnn, Yong-Sung
CORPORATE SOURCE: Dep. Biochemistry, Seoul Natl. Univ. Coll. Med., Seoul 110-799 South Korea
SOURCE: Experimental & Molecular Medicine, (Dec. 31, 1997) Vol. 29, No. 4, pp. 223-227.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Some malignant melanoma cells regress spontaneously by terminal differentiation, and understanding the mechanisms of this spontaneous regression can contribute to the development of a new therapy not only for melanoma but also for other cancers. The signal transducing G protein is one component of the signaling pathways for the differentiation-inducing molecules such as alpha- ***melanocyte*** - ***stimulating*** ***hormone*** (alpha-MSH) and ***cAMP*** . To investigate the role of G proteins in the differentiation process, we analyzed the expression of various G proteins by quantitative Western blot and ***cAMP*** response in human malignant melanoma cell lines. SK-MEL-3 cells expressed the largest amount of stimulatory G protein alpha subunit (Gsalpha) and the largest amount of ***inhibitory*** G protein alpha subunit (Glalpha) was expressed in Malme-3M cells among the 4 melanoma cell lines analyzed in this experiment. The SK-MEL-28 cells exhibited largest amount of alpha subunit of Gq and the bets subunits. The ***cAMP*** formation by forskolin stimulation was largest in the Malme-3M. The amount of ***cAMP*** formation did not show any correlation with the expression of Gsalpha nor that of Glalpha. The population doubling time we found that the melanoma cells vary widely both in the expression of various G proteins and in ***cAMP*** ***production*** depending on the cell lines.

L11 ANSWER 7 OF 25 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 97009393 MEDLINE
DOCUMENT NUMBER: 97009393 PubMed ID: 8856498
TITLE: Induction of constitutive melanogenesis in amelanotic mouse melanoma cells by transfection of the human melanocortin-1 receptor gene.
AUTHOR: Chluba-de Tapia J; Bagutti C; Cotti R; Eberle A N
CORPORATE SOURCE: Department of Research (ZLF), University Hospital, Basel, Switzerland.
SOURCE: JOURNAL OF CELL SCIENCE, (1996 Aug) 109 ( Pt 8) 2023-30. Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970313
Last Updated on STN: 19970313
Entered Medline: 19970303
AB The human melanocortin-1 (MC1) receptor was stably expressed in the amelanotic mouse melanoma cell clone B16-G4F which does not express its own (mouse) MC1 receptor and hence is unresponsive to alpha ***melanocyte*** ***stimulating*** ***hormone*** (alpha MSH).

From several stable transfectant cell lines expressing the human MC1 receptor in relatively high numbers, three melanin ***producing*** clones (G4F-12, 14, and 15) and one amelanotic clone (G4F-7) were further analyzed in competition binding experiments and in ***CAMP*** and melanin assays. The dissociation constants (KD) for [Nle4, D-Phe7]-alpha MSH in all four clones ranged from 0.187 to 0.705 nmol/l, thus corresponding to the KD observed with the different human melanoma cell lines so far studied. Intracellular ***CAMP*** content was 3- to 5-fold higher than that of control cells, and alpha MSH induced an additional 1.5- to 1.7-fold increase. G4F-15 cells secreted melanin into the medium whereas the other clones did not secrete melanin. The extent of melanin secretion was similar to that of fully alpha MSH-stimulated B16-F1 mouse melanoma cells but the onset of secretion was delayed. alpha MSH induced an additional dose-related increase (up to 1.3-fold) in melanin ***production*** which could be suppressed by the addition of specific alpha MSH antibodies without altering the constitutive part of melanogenesis. Human and mouse agouti proteins, which ***inhibit*** basal and alpha MSH-induced melanogenesis in B16-F1 cells, both reduced alpha MSH-induced melanin ***production*** in G4F-15 cells but did not affect the constitutive melanogenesis. These results indicate that human MC1 receptor expressed in mouse B16-G4F cells induces constitutive activation of the signalling pathway controlling melanogenesis, most likely by tightly coupling to Gs alpha, in a similar manner to that reported for constitutively active receptor mutants in other systems.

L11 ANSWER 8 OF 25 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 96396976 MEDLINE
DOCUMENT NUMBER: 96396976 PubMed ID: 8804079
TITLE: The neuropeptide alpha-MSH has specific receptors on neutrophils and reduces chemotaxis in vitro.
AUTHOR: Catania A; Rajora N; Capsoni F; Minonzio F; Star R A; Lipton J M
CORPORATE SOURCE: Institute of Internal Medicine, University of Milan, Italy.
CONTRACT NUMBER: NS10046 (NINDS)
SOURCE: PEPTIDES, (1996) 17 (4) 675-9.
Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970124

AB The proopiomelanocortin-derived peptide alpha- ***melanocyte*** ***stimulating*** ***hormone*** (alpha-MSH) has potent anti-inflammatory effects in all animal models of inflammation against which it has been tested. Understanding of the mechanism by which this occurs is incomplete, although there is recent evidence for alpha-MSH receptors in murine and human macrophages and for modulation of ***production*** of proinflammatory cytokines and related mediators by alpha-MSH. Because of the prominence of neutrophils in early stages of inflammatory reactions where alpha-MSH is effective, we examined human neutrophils for evidence of mRNA for alpha-MSH receptors and for ***inhibition*** of neutrophil chemotaxis. There was accumulation of mRNA for melanocortin receptor 1 (MC1) in RT/PCR ***product*** from neutrophils stimulated with interferon and LPS. In subsequent studies alpha-MSH ***inhibited*** migration of neutrophils from most normal volunteers when the cells were placed in FMLP or IL-8 gradients. The ***inhibition*** by alpha-MSH could be traced to alterations in ***CAMP*** in neutrophils. The presence of alpha-MSH receptor message in neutrophils is consistent with the established anti-inflammatory effects of the peptide. Direct ***inhibition*** of neutrophil chemotaxis likely contributes to the anti-inflammatory activity of alpha-MSH.

L11 ANSWER 9 OF 25 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 97021894 MEDLINE
DOCUMENT NUMBER: 97021894 PubMed ID: 8868254
TITLE: Adenosine inhibits L- and N-type calcium channels in pituitary melanotrophs. Evidence for the involvement of a G protein in calcium channel gating.
AUTHOR: Mei Y A; Le Foll F; Vaudry H; Cazin L
CORPORATE SOURCE: Laboratory of Cellular and Molecular Neuroendocrinology, INSERM U 413, University of Rouen, Mont-Saint-Aignan, France.
SOURCE: JOURNAL OF NEUROENDOCRINOLOGY, (1996 Feb) 8 (2) 85-91.

Journal code: 8913461. ISSN: 0953-8194.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 20021218
Entered Medline: 19961127

AB It has been previously demonstrated that activation of A1 adenosine receptors in frog melanotrophs causes ***inhibition*** of spontaneous action potential discharges and alpha- ***melanocyte*** - ***stimulating*** ***hormone*** secretion. In the present study, we have investigated the effect of adenosine on high-voltage-activated (HVA) calcium currents in cultured melanotrophs, using the whole-cell variant of the patch-clamp technique with barium as a charge carrier. Adenosine and the specific A1 adenosine receptor agonist R-PIA (50 microM each) ***produced*** a decrease of the amplitude of the barium current, while the selective A2 adenosine receptor agonist CGS 21680 did not affect the current. The ***inhibitory*** effect of R-PIA was observed throughout the activation range of the current, with stronger responses at more positive potentials. R-PIA ***inhibited*** both the L- and N-type components of the current, the effect on the N-component being two-fold higher than on the L-component. The ***inhibitory*** effect of R-PIA was rendered irreversible by addition of GTP gamma S (100 microM) to the intracellular solution. Pre-treatment of the cells with pertussis toxin (1 microgram/ml; 12 h) totally abolished the effect of R-PIA on the HVA calcium channels. Conversely, addition of a high concentration of ***cAMP*** (100 microM) together with the phosphodiesterase ***inhibitor*** IBMX (100 microM) to the intracellular solution did not modify the effect of R-PIA on the current. It is concluded that, in frog melanotrophs, adenosine induces ***inhibition*** of L- and N-calcium currents and that this effect is mediated by a pertussis toxin-sensitive G protein. Our data also indicate that the ***inhibitory*** effect of adenosine on the calcium currents is not mediated by ***inhibition*** of adenylyl cyclase.

L11 ANSWER 10 OF 25 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 95372410 MEDLINE
DOCUMENT NUMBER: 95372410 PubMed ID: 7544012
TITLE: Evidence of autocrine modulation of macrophage nitric oxide synthase by alpha-melanocyte-stimulating hormone.
AUTHOR: Star R A; Rajora N; Huang J; Stock R C; Catania A; Lipton J M
CORPORATE SOURCE: Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas 75235, USA.
CONTRACT NUMBER: DK-01888 (NIDDK)
NS10046 (NINDS)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Aug 15) 92 (17) 8016-20.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950930
Last Updated on STN: 19960129
Entered Medline: 19950921

AB alpha- ***Melanocyte*** - ***stimulating*** ***hormone*** (alpha-MSH) is a potent ***inhibitory*** agent in all major forms of inflammation. To identify a potential mechanism of antiinflammatory action of alpha-MSH, we tested its effects on ***production*** of nitric oxide (NO), believed to be a mediator common to all forms of inflammation. We measured NO and alpha-MSH ***production*** in RAW 264.7 cultured murine macrophages stimulated with bacterial lipopolysaccharide and interferon gamma. alpha-MSH ***inhibited*** ***production*** of NO, as estimated from nitrite ***production*** and nitration of endogenous macrophage proteins. This occurred through ***inhibition*** of ***production*** of NO synthase II protein; steady-state NO synthase II mRNA abundance was also reduced. alpha-MSH increased ***cAMP*** accumulation in RAW cells, characteristic of alpha-MSH receptors in other cell types. RAW cells also expressed mRNA for the primary alpha-MSH receptor (melanocortin 1). mRNA for proopiomelanocortin, the precursor molecular of alpha-MSH, was expressed in RAW cells, and tumor necrosis factor alpha increased ***production*** and release of alpha-MSH. These results suggest that the proinflammatory

cytokine tumor necrosis factor alpha can induce macrophages to increase ***production*** of alpha-MSH, which then becomes available to act upon melanocortin receptors on the same cells. Such stimulation of melanocortin receptors could modulate inflammation by ***inhibiting*** the ***production*** of NO. The results suggest that alpha-MSH is an autocrine factor in macrophages which modulates inflammation by counteracting the effects of proinflammatory cytokines.

L11 ANSWER 11 OF 25 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 95240364 MEDLINE
DOCUMENT NUMBER: 95240364 PubMed ID: 7723599
TITLE: Pyrroloquinoline quinone (PQQ) inhibits the expression of tyrosinase mRNA by alpha-melanocyte stimulating hormone in murine B16 melanoma cells.
AUTHOR: Kosano H; Setogawa T; Kobayashi K; Nishigori H
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Teikyo University, Kanagawa, Japan.
SOURCE: LIFE SCIENCES, (1995) 56 (20) 1707-13.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950605
Last Updated on STN: 19970203
Entered Medline: 19950525
AB The biological functions of pyrroloquinoline quinone (PQQ), a bacterial redox coenzyme and potent radical scavenger, have not been elucidated in mammals. In this paper, we studied the effects of PQQ on tyrosinase activity and subsequent melanogenesis in murine B16-F10 melanoma and found that alpha- ***Melanocyte*** ***stimulating*** ***hormone*** (MSH)-induced melanogenesis was ***inhibited*** by 6.3 to 25 microM PQQ in a dose-dependent manner. Moreover, PQQ ***inhibited*** MSH-induced tyrosinase activity by suppressing tyrosinase mRNA expressed by MSH. However, PQQ had no effect on MSH-stimulated cyclic adenosine 3', 5'-monophosphate ( ***cAMP*** ) ***production*** . These observations suggest that PQQ ***inhibits*** the expression of tyrosinase mRNA at a post receptor level and that PQQ may be useful in investigating hormone actions mediated by ***cAMP*** .

L11 ANSWER 12 OF 25 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 95252807 MEDLINE
DOCUMENT NUMBER: 95252807 PubMed ID: 7734952
TITLE: Impairment of the melanogenic pathway in B16 melanoma cells transfected with class I H-2 genes.
AUTHOR: Prezioso J A; Hearing V J; Muller J; Urabe K; Wang N; Gorelik E
CORPORATE SOURCE: Department of Radiation Oncology, University of Pittsburgh, Pittsburgh Cancer Institute, PA, USA.
SOURCE: MELANOMA RESEARCH, (1995 Feb) 5 (1) 15-25.
Journal code: 9109623. ISSN: 0960-8931.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950615
Last Updated on STN: 19970203
Entered Medline: 19950608
AB Transfection of class I H-2Kb or H-2Kd into cells of a pigmented subclone of B16-F10 BL6 (termed BL6-8) results in the loss of melanin ***production*** . In contrast, transfected BL6-8 cells expressing H-2Dd, H-2Ld, class I H-21Ak and/or the neor genes maintained their pigmented phenotype. Melanogenesis was also ***inhibited*** in cells which expressed the endogenous H-2Kb, but not the endogenous H-2Db, gene. In order to identify the specific defects in the melanogenic pathway responsible for the absence of melanin ***production*** , factors known to be related to the regulation of pigment formation were evaluated in H-2K-expressing cells. These studies showed that: (1) transfection of BL6-8 cells with the H-2Kb or H-2Kd, but not with the H-2Dd, H-2Ld or H-21Ak, genes was associated with complete ***inhibition*** of tyrosinase activity; (2) alpha- ***melanocyte*** - ***stimulating*** ***hormone*** (MSH) and theophylline (an ***inhibitor*** of ***cAMP*** phosphodiesterase) failed to stimulate tyrosinase activity in H-2K-positive cells, whereas tyrosinase activities in untransfected, or H-2DdH-2Ld, neor or H-21Ak-transfected cells were dramatically increased

by those agents; (3) treatment with MSH had no effect on ***cAMP*** levels in H-2K-positive cells but stimulated ***cAMP*** levels more than 100-fold in H-2K-negative cells; (4) in contrast to MSH, forskolin, a stimulator of adenylate cyclase, was able to stimulate ***cAMP*** levels in all cell lines tested, but in H-2Kb-positive cells the levels of forskolin-induced ***cAMP*** were significantly less than those elicited in H-2Kb-negative cells; (5) electron microscopy showed that H-2K-positive cells lacked mature melanosomes; (6) Northern blot analyses showed that H-2K-positive cells lacked mRNA for tyrosinase or for the MSH receptor. Taken together, expression of the endogenous or transfected H-2K gene in BL6 melanoma cells results in down-regulation of the entire melanogenic pathway, including the ***inhibition*** of tyrosinase and MSH receptor gene expression, ***cAMP*** responses and melanosomal biogenesis.

L11 ANSWER 13 OF 25 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 93232728 MEDLINE
DOCUMENT NUMBER: 93232728 PubMed ID: 8386214
TITLE: Effect of dopamine on adenylate cyclase activity, polyphosphoinositide metabolism and cytosolic calcium concentrations in frog pituitary melanotrophs.
AUTHOR: Desrues L; Lamacz M; Jenks B G; Vaudry H; Tonon M C
CORPORATE SOURCE: European Institute for Peptide Research, CNRS URA 650, UA INSERM, University of Rouen, Mont-Saint-Aignan, France.
SOURCE: JOURNAL OF ENDOCRINOLOGY, (1993 Mar) 136 (3) 421-9.
Journal code: 0375363. ISSN: 0022-0795.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930604
Last Updated on STN: 19980206
Entered Medline: 19930517

AB It has previously been shown that dopamine plays a pivotal role in the regulation of alpha- ***melanocyte*** - ***stimulating*** ***hormone*** (alpha-MSH) secretion from the intermediate lobe of the pituitary. In the present study, we have investigated the various intracellular mechanisms that are associated with the action of dopamine on frog pituitary melanotrophs. Dopamine reduced forskolin-stimulated cyclic adenosine monophosphate ( ***cAMP*** ) ***production*** and the ***inhibitory*** effect of dopamine was blocked by the dopaminergic D2 receptor antagonist sulpiride. The D2 receptor agonist apomorphine ***inhibited*** incorporation of [3H]inositol into membrane phospholipids. Dopamine also ***inhibited*** the formation of inositol trisphosphate and provoked accumulation of phosphatidylinositol bisphosphate. The ***inhibitory*** effect of dopamine on inositol trisphosphate ***production*** was mimicked by D2 receptor agonists and blocked by sulpiride. Using a double-wavelength microfluorimetric approach, we found that dopamine caused a rapid and transient decrease in K(+)-evoked stimulation of intracellular calcium concentration. The time-courses of the responses of the various intracellular messengers indicate that blockage of voltage-dependent calcium channels is the primary event associated with activation of dopamine D2 receptors, while ***inhibition*** of polyphosphoinositide breakdown, related to blockage of voltage-dependent calcium channels, and reduction of ***cAMP*** ***production*** are secondary events which may contribute to the sustained ***inhibitory*** effect of dopamine on alpha-MSH release.

L11 ANSWER 14 OF 25 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 89325839 MEDLINE
DOCUMENT NUMBER: 89325839 PubMed ID: 2546842
TITLE: Adrenocorticotropic hormone inhibits angiotensin II-stimulated inositol phosphate accumulation in rat adrenal glomerulosa cells.
AUTHOR: Woodcock E A
CORPORATE SOURCE: Monash University Department of Medicine, Prince Henry's Hospital, Melbourne, Australia.
SOURCE: MOLECULAR AND CELLULAR ENDOCRINOLOGY, (1989 May) 63 (1-2) 247-53.
Journal code: 7500844. ISSN: 0303-7207.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908

ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890831

AB Rat adrenal glomerulosa cells labelled for 18 h with [3H]inositol responded to angiotensin II with a dose-dependent stimulation of the accumulation of inositol monophosphate, inositol bisphosphate and inositol trisphosphate. Addition of adrenocorticotropic hormone (ACTH) (10(-7)M) reduced the maximum responses without altering the EC50 values for angiotensin II. Thus, ACTH acted as a non-competitive ***inhibitor*** with respect to angiotensin II. No ***inhibition*** was observed in cells labelled for 2 h with [3H]inositol. Detailed examination of the ***inhibition*** showed that ACTH(1-24) was the most potent ***inhibitor*** , with ACTH(1-39) being 10-fold less potent. A mixture of alpha- ***melanocyte*** - ***stimulating*** ***hormone*** (alpha-MSH) (ACTH(1-13] and corticotropin-like intermediate lobe peptide (ACTH(18-39] was similarly inactive. ACTH(5-24) did not ***produce*** detectable ***inhibition*** . In terms of specificity, the receptor mediating ACTH ***inhibition*** of phosphatidylinositol turnover was similar to the receptor which mediated stimulation of aldosterone synthesis. ***Inhibition*** by ACTH was additive with ***inhibition*** ***produced*** by dibutyryl ***CAMP*** demonstrating that it was not mediated by rises in intracellular ***CAMP*** . ACTH ***inhibition*** also was additive with ***inhibition*** by the calcium channel blocker, nifedipine. These results demonstrate an interaction between ACTH receptors and angiotensin II receptors in adrenal glomerulosa cells at the level of their receptor-second messenger pathways.

L11 ANSWER 15 OF 25 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 87260965 MEDLINE
DOCUMENT NUMBER: 87260965 PubMed ID: 3037540
TITLE: Regulation of cell shape in the Cloudman melanoma cell line.
AUTHOR: Preston S F; Volpi M; Pearson C M; Berlin R D
CONTRACT NUMBER: CA-15544 (NCI)
GM-30209 (NIGMS)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1987 Aug) 84 (15) 5247-51.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198708
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19870826

AB We show that Cloudman melanoma cells undergo rapid arborization in response to [Nle4,D-Phe7]alpha- ***melanocyte*** - ***stimulating*** ***hormone*** , a potent analogue of alpha- ***melanocyte*** ***stimulating*** ***hormone*** (alpha-MSH). The arbors were established by extension of processes and resembled dendrites. We used this system to study the regulation of cell shape. alpha-MSH is known to induce increases in ***CAMP*** levels, and agents such as forskolin and isobutylmethylxanthine that led to increased ***CAMP*** also caused arborization. However, equally dramatic arbors were formed after incubation with the protein kinase C ***inhibitor*** H-7 [1-(5-isoquinolinesulfonyl)-alpha-methyl-piperazine]. Phorbol diesters that activate protein kinase C led to cell rounding and antagonized alpha-MSH. The actions of protein kinase C cannot be rationalized in terms of indirect effects on ***CAMP*** : neither H-7 nor phorbol diesters alone altered ***CAMP*** levels, nor did they affect the increase in ***CAMP*** induced by MSH. We show also that MSH ***produced*** longer-term effects that cannot be mimicked by ***CAMP*** . Specifically, even in the continued presence of alpha-MSH, arborization was followed by morphological reversal to the unstimulated flattened configuration within 2 hr. (This did not occur with other agents that increase ***CAMP*** or with H-7.) Most importantly, whereas MSH-induced arborization occurred in the presence of cycloheximide, actinomycin D, or in enucleated cells, the reversal of arborization did not. Thus, MSH induced a program of rapid shape change that was dependent on new protein synthesis and gene transcription.

L11 ANSWER 16 OF 25 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 83136010 MEDLINE
DOCUMENT NUMBER: 83136010 PubMed ID: 6826662
TITLE: Specific protein production during melanogenesis in B16/C3

melanoma cells.
AUTHOR: Laskin J D; Piccinini L; Engelhardt D L; Weinstein I B
SOURCE: JOURNAL OF CELLULAR PHYSIOLOGY, (1983 Jan) 114 (1) 68-72.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198304
ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 19900318
Entered Medline: 19830415

AB The mouse melanoma cell line B16/C3 offers an excellent in vitro model for studying melanocyte differentiation. Melanogenesis can be induced by serum, a hormone-supplemented serum-free medium, ***melanocyte*** ***stimulating*** ***hormone*** , and dibutyryl ***CAMP*** . The tumor promoter, 12-O-tetradecanoyl-phorbol-13-acetate, 5-bromodeoxyuridine, and acidic pH ***inhibit*** this process. Using two-dimensional polyacrylamide gel electrophoresis, we have identified four cellular proteins whose ***production*** is modulated during melanogenesis, a process which includes concomitant increases in levels of tyrosinase, the rate limiting enzyme for melanin biosynthesis, melanization, and ultimately, cell death. The ***production*** of these proteins are coordinately expressed or ***inhibited*** in response to the diverse inducers and ***inhibitors*** of melanogenesis. We conclude from these studies that these specific proteins are intimately involved in the differentiation of B16/C3 melanoma cells.

L11 ANSWER 17 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1981:162630 BIOSIS
DOCUMENT NUMBER: BA71:32622
TITLE: STIMULATION OF MELANOGENESIS IN A HUMAN MELANOMA CELL LINE BY RETINOIDS.
AUTHOR(S): LOTAN R; LOTAN D
CORPORATE SOURCE: DEP. BIOPHYS., WEIZMANN INST. SCI., REHOVOT, ISR.
SOURCE: CANCER RES, (1980) 40 (9), 3345-3350.
CODEN: CNREA8. ISSN: 0008-5472.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Retinoic acid was a potent stimulant of pigmentation in human Hs939 melanoma cells. Exposure to 1 .mu.M retinoic acid for longer than 4 days caused a decrease in the rate of cell proliferation and a concomitant increase in melanogenesis. These effects of retinoic acid progressed linearly in a time-dependent and a dose-dependent fashion, such that at the end of a 7 day treatment cell growth was ***inhibited*** by approximately 65%; melanin content and tyrosinase activity increased more than 3-fold over the control. Interpolation of the dose-response curves indicated that 3 nM retinoic acid would cause half-maximal melanogenesis stimulation. No elevation in the level of ***CAMP*** was detected in the melanoma cells following various periods of exposure to retinoic acid; the cells were unresponsive to .alpha.- ***melanocyte*** - ***stimulating*** ***hormone*** . In the presence of the tyrosinase ***inhibitor*** phenylthiocarbamate, retinoic acid was capable of ***inhibiting*** cell proliferation without enhancing melanin synthesis. The tumor promoter phorbol myristate acetate did not affect the proliferation or the differentiation of the Hs939 melanoma cells. The enhancement of melanogenesis by 1 .mu.M retinoic acid was ***inhibited*** by 66% in the presence of 0.1 .mu.M phorbol myristate acetate. The tumor promoter did not reverse the growth- ***inhibitory*** effect of retinoic acid. Phorbol, a non-tumor promoter, was ineffective. Other retinoids, such as 13-cis-retinoic acid, retinyl acetate and the trimethylmethoxyphenyl analog of retinoic acid, also ***inhibited*** the proliferation and enhanced melanin ***production*** in the Hs939 cells. Retinyl palmitate, the phenyl analog of retinoic acid, and the pyridyl analog of retinoic acid were ineffective.

L11 ANSWER 18 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1980:278154 BIOSIS
DOCUMENT NUMBER: BA70:70650
TITLE: IN-VITRO MITOGENIC AND STEROIDOGENIC EFFECTS OF ACTH ANALOGS ON AN ADRENAL TUMOR CELL LINE Y-1.
AUTHOR(S): MORERA A M; SAEZ J M
CORPORATE SOURCE: UNITE RECH. CONTROL HORM. ACT. CELL., INST. NATL. SANTE RECH. MED.,, HOP. DEBROUSSE, 69322 LYON CEDEX 1, FRANCE.
SOURCE: EXP CELL RES, (1980) 127 (2), 446-451.
CODEN: ECREAL. ISSN: 0014-4827.

FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Native porcine ACTH1-39 and synthetic ACTH1-24 increase c[cyclic]AMP and steroid ***production*** and ***inhibit*** DNA synthesis in [mouse Y-1] adrenal cell line. The COOH terminal sequence of both peptides and .beta.-endorphin have no effects, while the NH2 terminal sequence of ACTH and .alpha.-MSH [ ***melanocyte*** ***stimulating*** ***hormone*** ] which have very low stimulatory effect on ***cAMP*** ***production*** , have a mitogenic effect. ACTH might have some mitogenic action on adrenal cell in vitro, but this effect is blunted by ***cAMP*** accumulation during hormonal stimulation. The results can also explain the in vivo and in vitro contradictory effects of the hormone on adrenal cell replication.

L11 ANSWER 19 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1980:286881 BIOSIS
DOCUMENT NUMBER: BA70:79377
TITLE: DECAY OF HORMONE RESPONSIVENESS IN MOUSE MELANOMA CELLS IN CULTURE AS A FUNCTION OF CELL DENSITY.
AUTHOR(S): FULLER B B; LEBOWITZ J
CORPORATE SOURCE: DEP. GEN. BIOL., UNIV. ARIZ., TUCSON, ARIZ. 85721, USA.
SOURCE: J CELL PHYSIOL, (1980) 103 (2), 279-288.
CODEN: JCLLAX. ISSN: 0021-9541.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Cloudman S91 mouse melanoma cells lose their ability to demonstrate an MSH[ ***melanocyte*** ***stimulating*** ***hormone*** ]-induced increase in tyrosinase activity as cell density increases. This loss in hormone responsiveness occurs before confluency is reached and cannot be reversed by exposing cells to increasing concentrations of MSH. The failure of high-density cultures to respond to MSH is apparently not the result of an inability of MSH to stimulate c[cyclic]AMP ***production*** , since either low- or high-density cultures exposed to MSH demonstrate equivalent increases in intracellular levels of ***cAMP*** . Theophylline (1 mM), dibutyryl ***cAMP*** (10-4 M) and prostaglandin E1 (10-6 M) each failed to stimulate tyrosinase activity in melanoma cells cultured at densities exceeding 6 .times. 104 cells/cm2. The decay of hormone responsiveness apparently occurs at a cellular site distal to ***cAMP*** ***production*** . The decrease in tyrosinase stimulation by MSH as cell density increases is also apparently not the result of an increase in activity of any soluble ***inhibitor*** of the enzyme; cytosol preparations from high-density cultures (105 cells/cm2) fail to ***inhibit*** tyrosinase activity in cell homogenates from low-density cultures treated with MSH.

L11 ANSWER 20 OF 25 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 78244711 MEDLINE
DOCUMENT NUMBER: 78244711 PubMed ID: 210294
TITLE: Control of melanogenesis in mouse melanoma cells of varying metastatic potential.
AUTHOR: Niles R M; Makarski J S
SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1978 Aug) 61 (2) 523-6.
Journal code: 7503089. ISSN: 0027-8874.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197810
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19781025
AB The control of melanin ***production*** , tyrosinase activity, and cell replication by ***melanocyte*** - ***stimulating*** ***hormone*** (MSH) and cyclic AMP ( ***cAMP*** ) was examined in differentially metastasizing B16 mouse melanoma variants. In B16-F1 cells (low metastatic potential), MSH or ***cAMP*** greatly elevated tyrosinase activity and melanin content while ***inhibiting*** cell replication. The same parameters in B16-F5 cells (intermediate metastatic potential) were altered to a much lesser degree, whereas B16-F10 cells (high metastatic potential) were not significantly affected by MSH or ***cAMP*** . Therefore, a correlation exists between loss of hormonal regulation and increased metastatic potential.

L11 ANSWER 21 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1978:209193 BIOSIS
DOCUMENT NUMBER: BA66:21690

TITLE: THE EFFECT OF THE DIVALENT CATION IONOPHORE A-23187 ON AMPHIBIAN MELANOPHORES AND IRIDOPHORES.
AUTHOR(S): NOVALES R R
CORPORATE SOURCE: DEP. BIOL. SCI., NORTHWEST. UNIV., EVANSTON, ILL. 60201, USA.
SOURCE: J INVEST DERMATOL, (1977) 69 (5), 446-450.
CODEN: JIDEAE. ISSN: 0022-202X.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Ca2+ ions are required in the medium for the full darkening action of ***melanocyte*** - ***stimulating*** ***hormone*** , but not for its second messenger, cyclic[c]AMP, on isolated frog skin. The possible effect of the divalent cation ionophore A23187 was studied, using the skin of Rana pipiens. It is a potent darkening agent over the range of 1-2 .mu.M, as measured by reflectance change and microscopic observation. During the darkening response to A23187, melanosome dispersion takes place in both dermal and epidermal melanophores, as well as aggregation of iridophore reflecting platelets. The darkening is slowly reversible in Ringer's solution, thus it is not due to toxicity. The darkening is partially dependent on the presence of Ca in the medium under certain conditions, suggesting that the response involves both the uptake and release of Ca ions. Cytochalasin B reversibly ***inhibits*** the darkening ***produced*** by A23187. Since this drug is known to bring about the breakdown of microfilaments, its ***inhibitory*** action is in accord with the concept that the ionophore is stimulating microfilament function. A23187 administered to tissue cultured embryonic salamander (Ambystoma maculatum) melanophores ***produced*** an irreversible rounding up of the cells, suggesting a toxic effect. The results with frog skin are interpreted as supporting the concept that the action of ***melanocyte*** - ***stimulating*** ***hormone*** involves the ***production*** of pigment granule movements as a result of the interaction of Ca ions with intracellular microfilaments and possible also the breakdown of microtubules. The mobilization of Ca ions could be brought about by ***cAMP*** .

L11 ANSWER 22 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 18
ACCESSION NUMBER: 1978:141142 BIOSIS
DOCUMENT NUMBER: BA65:28142
TITLE: THE DUAL EFFECT OF MELANOCYTE STIMULATING HORMONE ON THE GROWTH OF CULTURED MOUSE MELANOMA CELLS.
AUTHOR(S): HALABAN R; LERNER A B
CORPORATE SOURCE: DEP. DERMATOL., YALE UNIV. SCH. MED., NEW HAVEN, CONN. 06510, USA.
SOURCE: EXP CELL RES, (1977) 108 (1), 111-118.
CODEN: ECREAL. ISSN: 0014-4827.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Melanotropin ( ***melanocyte*** - ***stimulating*** ***hormone*** , MSH) can stimulate or ***inhibit*** the rate of proliferation of melanocytes. Stimulation was observed in cultures of mouse melanoma cells that had low tyrosinase activity and in cells that had normal tyrosinase activity but were grown in medium that was changed frequently or was deficient in tyrosine. ***Inhibition*** of growth was associated with high tyrosinase activity and the presence of tyrosine in the culture medium. Small amounts of exogenous cyclic [c] AMP stimulate the growth rate of these cells. Since MSH causes an increase in intracellular levels of ***cAMP*** it is likely that the stimulation of growth is due to the ability of this hormone to increase the intracellular levels of ***cAMP*** . ***Inhibition*** of growth in turn is related to the activation of tyrosinase by MSH and the accumulation of toxic stubstances ***produced*** by the tyrosinase reaction.

L11 ANSWER 23 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 78018027 EMBASE
DOCUMENT NUMBER: 1978018027
TITLE: Ionophore A23187 and dibutyryl cyclic AMP effects on cell shape and morphology of B 16 melanoma.
AUTHOR: Sauk Jr. J.J.
CORPORATE SOURCE: Div. Hum. Oral Genet. Oral Pathol., Univ. Minnesota, Minneapolis, Minn. 55455, United States
SOURCE: Virchows Archiv Abteilung B Cell Pathology, (1976) 22/4 (305-313).
CODEN: VAAZA2
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
005 General Pathology and Pathological Anatomy

016 Cancer
013 Dermatology and Venereology
LANGUAGE: English
AB Melanoma cells in culture possess various shapes depending on the stage of the cell cycle. Stimulation by ***melanocyte*** ***stimulating*** ***hormone*** (MSH) resulting in elevation of cyclic AMP ( ***cAMP*** ) growth ***inhibition*** and melanin synthesis will stabilize these cells in a morphology characterized by the presence of long dendrites. The dendrites of melanoma cells have been shown to contain assembled and paralleled aligned microtubules and microfilaments. The ionophore A23187 is a carboxylic acid derivative which has a high affinity for calcium and a diminished attraction to other divalent events dependent on elevation of cytosolic calcium. Recently this compound has been shown to ***inhibit*** butyrate and dibutyryl ***cAMP*** (db ***cAMP*** ) induced cell morphologies in HeLa and CHO cells. Treatment of B16 melanoma cells with (db ***cAMP*** ) for 24 hr resulted in dendritic cells possessing parallel assembled microtubules. A23187 treatment resulted in a biphasic response: its long term effect was characterized by small epithelioid cells, while the immediate response ***produced*** elongated cells with parallel arranged 10 nm mocrofilaments, characteristic of dispersive melanocytes.

L11 ANSWER 24 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1976:202626 BIOSIS
DOCUMENT NUMBER: BA62:32626
TITLE: FACTORS REGULATING GROWTH AND PIGMENTATION OF MELANOMA CELLS.
AUTHOR(S): PAWELEK J M
SOURCE: J INVEST DERMATOL, (1976) 66 (4), 201-209.
CODEN: JIDEAE. ISSN: 0022-202X.
FILE SEGMENT: BA; OLD
LANGUAGE: Unavailable
AB Growth and melanization are intimately related in melanoma cells. MSH [ ***melanocyte*** ***stimulating*** ***hormone*** ], by promoting elevated c(cyclic)AMP levels, causes increases in melanization, cessation of growth and gross morpholgic changes in Cloudman S-91 mouse melanoma cells. Growth ***inhibition*** results from high levels of ***cAMP*** while growth stimulation occurs with lower levels. During melanization, oxidation ***products*** of tyrosine are generated which are toxic to the cells. Genetic studies revealed that some of these processes are related through common biochemical pathways. This article reviews work of recent years on such regulatory mechanisms in melanoma.

L11 ANSWER 25 OF 25 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 76071502 MEDLINE
DOCUMENT NUMBER: 76071502 PubMed ID: 172624
TITLE: Effects of choroid plexus peptide IIF on adenylate cyclase and 3',5'-cyclic adenosine monophosphate in adipose tissue.
AUTHOR: Rudman D
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1975 Dec) 195 (3) 532-9.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197602
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19980206
Entered Medline: 19760227
AB Two hypophyseal lipolytic peptides, adrenocorticotropin (ACTH) and beta- ***melanocyte*** - ***stimulating*** ***hormone*** (beta-MSH), and the extrhypophyseal lipolytic peptide IIF, were compared with regard to their effects on free fatty acid ***production*** and 3',5'-cyclic adenosine monophosphate ( ***cAMP*** ) concentration in isolated rabbit and rat adipose tissue, and on adenylate cyclase activity in the tissue homogenates. ACTH at concentrations of 0.01 mug/ml or more increased lipolysis and ***cAMP*** levels in both tissues. beta-MSH at concentrations of 0.001 mug/ml or more increased lipolysis and ***cAMP*** in the rabbit tissue, but a concentration of 10 mug/ml did not stimulate lipolysis and did not alter nucleotide concentration in the rat tissue. Peptide IIF at 0.01 mug/ml or more stimulated lipolysis in rabbit adipose tissue and caused an accumulation of ***cAMP*** . A concentration of 100 mug/ml failed to stimulate free fatty acid ***production*** in the rat tissue and the ***cAMP*** level was also unaffected. In a medium containing 7.6 mEq/l of Mg++ and no Ca++, ACTH at 0.1 mug/ml or more stimulated adenylate cyclase activity in both rabbit

and rat adipose homogenates by 6- to 12-fold. This effect was ***inhibited*** when Mg++ was replaced by Ca++, Na+ or K+. beta-MSH stimulated adenylate cyclase in rabbit, but not in rat, adipose homogenate in Mg++-containing incubation midium; again, the effect on rabbit adenylate cyclase was suppressed when Mg++ was replaced by Ca++, Na+ or K+. Peptide IIF failed to influence adenylate cyclase in the rabbit tissue homogenate in the Mg++-containing, Ca++-free medium; but when the medium contained 7.6 mEq/l of Ca++ in place of Mg++, 0.1 mug/ml or more of IIF caused a 4- to 15-fold increase in cyclase activity. IIF did not affect cyclase in the rat tissue homogenate in the presence or absence of Ca++. The data are consistent with the conclusion that extrahypophyseal lipolytic peptide IIF, as well as hypophyseal peptides ACTH and beta-MSH, accelerates lipolysis in susceptible adipocytes by stimulating adenylate cyclase to ***produce*** ***cAMP*** . The effect of IIF on cyclase requires the presence of exogenous Ca++; that of ACTH and beta-MSH requires exogenous Mg++.

=> d his

(FILE 'HOME' ENTERED AT 19:31:37 ON 16 SEP 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 19:32:01 ON 16 SEP 2003

```
L1         11488 S MELANOCYTE STIMULATING HORMONE
L2          2488 S L1 (P) INHIBIT?
L3           224 S NAPHTHYL (P) (DIPEPTIDE OR TRIPEPTIDE)
L4             0 S L3 (P) L2
L5         69265 S CAMP (P) PRODUC?
L6            71 S L2 (P) L5
L7        122666 S IC50
L8             0 S L7 (P) L6
L9             6 S L6 (P) (50%) (P) INHIBIT?
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11           25 DUPLICATE REMOVE L6 (46 DUPLICATES REMOVED)
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=> s l3 (p) l5

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L12            1 L3 (P) L5
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=> d l1 1 ibib abs

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L1   ANSWER 1 OF 11488     MEDLINE on STN
ACCESSION NUMBER:   2003432535     IN-PROCESS
DOCUMENT NUMBER:    22854069   PubMed ID: 12972325
TITLE:              The central melanocortin system regulates food intake in
                    goldfish.
AUTHOR:             Cerda-Reverter Jose Miguel; Schioth Helgi Birgir; Peter
                    Richard Ector
CORPORATE SOURCE:   Department of Biological Sciences, University of Alberta,
                    T6G 2E9, Edmonton, Alberta, Canada.
SOURCE:             REGULATORY PEPTIDES, (2003 Sep 15) 115 (2) 101-13.
                    Journal code: 8100479. ISSN: 0167-0115.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:         Entered STN: 20030916
                    Last Updated on STN: 20030916
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AB Posttranscriptional processing of proopiomelanocortin (POMC) yields melanocortin peptides, which are involved in the regulation of energy balance in mammals. The sequence preservation of the main brain melanocortin, alpha- ***melanocyte*** - ***stimulating*** ***hormone*** (alpha-MSH), suggests a conserved function throughout vertebrate evolution. We studied the involvement of the central melanocortin system in the control of food intake in the goldfish. In situ hybridization studies done following molecular cloning of POMC mRNA demonstrated positive POMC mRNA cell bodies exclusively expressed within the mediobasal hypothalamus, in the anterior, posterior and inferior part of the lateral tuberal nucleus and the medial region of the lateral recess nucleus. POMC expression is localized in brain areas appropriate for involvement in food intake and neuroendocrine regulation. Progressive fasting did not affect POMC mRNA expression levels. Intracerebroventricular administration of [Nle(4), D-Phe(7)]-alpha-MSH (NDP-alpha-MSH), a universal melanocortin agonist, within nanomolar range, dose-dependently inhibited food intake 2 h after treatment. The results show for the first time a functional melanocortin system in fishes that participates in central regulation of food intake. The conserved central

expression pattern of POMC mRNA and role of MSH peptides in physiological regulation of food intake suggests that melanocortin functions were gained early in vertebrate evolution.

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     (FILE 'HOME' ENTERED AT 19:31:37 ON 16 SEP 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     19:32:01 ON 16 SEP 2003
L1         11488 S MELANOCYTE STIMULATING HORMONE
L2          2488 S L1 (P) INHIBIT?
L3           224 S NAPHTHYL (P) (DIPEPTIDE OR TRIPEPTIDE)
L4             0 S L3 (P) L2
L5         69265 S CAMP (P) PRODUC?
L6            71 S L2 (P) L5
L7        122666 S IC50
L8             0 S L7 (P) L6
L9             6 S L6 (P) (50%) (P) INHIBIT?
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11           25 DUPLICATE REMOVE L6 (46 DUPLICATES REMOVED)
L12            1 S L3 (P) L5

=> s whitening agent
L13         2419 WHITENING AGENT

=> s immuno? controlling agent
   4 FILES SEARCHED...
L14            1 IMMUNO? CONTROLLING AGENT

=> s appetite controlling agent
L15            1 APPETITE CONTROLLING AGENT

=> s cosmetic (p) (composition or preparation)
L16        25159 COSMETIC (P) (COMPOSITION OR PREPARATION)

=> s L13 or l14 or l15 or l16
L17        27531 L13 OR L14 OR L15 OR L16

=> s l17 and (l6 or l3)
L18            1 L17 AND (L6 OR L3)

=> d l18 1 ibib abs

L18  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2000:772657  CAPLUS
DOCUMENT NUMBER:          133:329599
TITLE:                    Melanocyte-stimulating hormone inhibitors
INVENTOR(S):              Shiojiri, Eiji; Takino, Yoshinobu; Chujou, Hiromi;
                          Sakamoto, Kazutami; Ijichi, Chiori; Eto, Yuzuru;
                          Iwasaki, Keiji
PATENT ASSIGNEE(S):       Ajinomoto Co., Inc., Japan
SOURCE:                   PCT Int. Appl., 37 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2000064926      A1   20001102       WO 2000-JP2687   20000425
         W:  CN, JP, KR, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     EP 1174437         A1   20020123       EP 2000-917447   20000425
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
PRIORITY APPLN. INFO.:                    JP 1999-118633   A  19990426
                                          WO 2000-JP2687   W  20000425
AB   MSH inhibitors characterized by contg., as the active ingredient, di- or
       ***tripeptide***   derivs. having a specific   ***naphthyl***   group or
     salts thereof, or a MSH inhibiting compd. showing a 50% inhibitory concn.
     (IC50) on cAMP prodn. of 100 nm or less.  These inhibitors can inhibit
     pigmentation, prevent, ameliorate or treat immunopathy or
     immunodeficiency, or regulate body wt. by controlling appetite.  These
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inhibitors are usable in ***cosmetics*** and skin ***prepns*** . for external use. Moreover, they can be easily produced and have a high storage stability.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 19:31:37 ON 16 SEP 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 19:32:01 ON 16 SEP 2003
L1 11488 S MELANOCYTE STIMULATING HORMONE
L2 2488 S L1 (P) INHIBIT?
L3 224 S NAPHTHYL (P) (DIPEPTIDE OR TRIPEPTIDE)
L4 0 S L3 (P) L2
L5 69265 S CAMP (P) PRODUC?
L6 71 S L2 (P) L5
L7 122666 S IC50
L8 0 S L7 (P) L6
L9 6 S L6 (P) (50%) (P) INHIBIT?
L10 2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11 25 DUPLICATE REMOVE L6 (46 DUPLICATES REMOVED)
L12 1 S L3 (P) L5
L13 2419 S WHITENING AGENT
L14 1 S IMMUNO? CONTROLLING AGENT
L15 1 S APPETITE CONTROLLING AGENT
L16 25159 S COSMETIC (P) (COMPOSITION OR PREPARATION)
L17 27531 S L13 OR L14 OR L15 OR L16
L18 1 S L17 AND (L6 OR L3)

=> s L17 AND 12
L19 2 L17 AND L2

=> duplicate remove 119
PROCESSING COMPLETED FOR L19
L20 2 DUPLICATE REMOVE L19 (0 DUPLICATES REMOVED)

=> s 120 not 118
L21 1 L20 NOT L18

=> d 121 1 ibib abs

L21 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:587233 CAPLUS
DOCUMENT NUMBER: 135:157403
TITLE: .alpha.-MSH inhibitors and their use for skin-lightening ***cosmetics*** and topical ***preparations***
INVENTOR(S): Tada, Akihiro; Kato, Tomomi; Katagiri, Takayuki
PATENT ASSIGNEE(S): Pola Chemical Industries, Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2001220347 | A2 | 20010814 | JP 2000-31260 | 20000209 |

PRIORITY APPLN. INFO.: JP 2000-31260 20000209
OTHER SOURCE(S): MARPAT 135:157403
GI

/ Structure 1 in file .gra /

AB Title inhibitors I (R1 = alkenyl; R2-R5 = OH, C1-4 alkyloxy, C1-4 acyloxy) and/or their physiol. acceptable salts are useful for skin-lightening cosmetics and for treatment of abnormal skin pigmentation in inflammation and/or immune diseases. Thus, sophoraflavanone G at 15 mM remarkably inhibited .alpha.-MSH.

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=> d his

     (FILE 'HOME' ENTERED AT 19:31:37 ON 16 SEP 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     19:32:01 ON 16 SEP 2003
L1         11488 S MELANOCYTE STIMULATING HORMONE
L2          2488 S L1 (P) INHIBIT?
L3           224 S NAPHTHYL (P) (DIPEPTIDE OR TRIPEPTIDE)
L4             0 S L3 (P) L2
L5         69265 S CAMP (P) PRODUC?
L6            71 S L2 (P) L5
L7        122666 S IC50
L8             0 S L7 (P) L6
L9             6 S L6 (P) (50%) (P) INHIBIT?
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11           25 DUPLICATE REMOVE L6 (46 DUPLICATES REMOVED)
L12            1 S L3 (P) L5
L13         2419 S WHITENING AGENT
L14            1 S IMMUNO? CONTROLLING AGENT
L15            1 S APPETITE CONTROLLING AGENT
L16        25159 S COSMETIC (P) (COMPOSITION OR PREPARATION)
L17        27531 S L13 OR L14 OR L15 OR L16
L18            1 S L17 AND (L6 OR L3)
L19            2 S L17 AND L2
L20            2 DUPLICATE REMOVE L19 (0 DUPLICATES REMOVED)
L21            1 S L20 NOT L18

=> s shiojiri eiji/au
L22           19 SHIOJIRI EIJI/AU

=> s takino yoshinobu/au
L23           14 TAKINO YOSHINOBU/AU

=> s chujou hiromi/au
L24            1 CHUJOU HIROMI/AU

=> s sakamoto kazutami/au
L25           80 SAKAMOTO KAZUTAMI/AU

=> s ljichi chiori/au
L26            0 LJICHI CHIORI/AU

=> s eto yuzuru/au
L27          119 ETO YUZURU/AU

=> s iwasaki keiji/au
L28           68 IWASAKI KEIJI/AU

=> s l22 or l23 or l24 or l25 or l27 or l28
L29          271 L22 OR L23 OR L24 OR L25 OR L27 OR L28

=> s l29 and (l2 or l3 or l6)
L30            1 L29 AND (L2 OR L3 OR L6)

=> s l30 not l18
L31            0 L30 NOT L18

=> d his

     (FILE 'HOME' ENTERED AT 19:31:37 ON 16 SEP 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     19:32:01 ON 16 SEP 2003
L1         11488 S MELANOCYTE STIMULATING HORMONE
L2          2488 S L1 (P) INHIBIT?
L3           224 S NAPHTHYL (P) (DIPEPTIDE OR TRIPEPTIDE)
L4             0 S L3 (P) L2
L5         69265 S CAMP (P) PRODUC?
L6            71 S L2 (P) L5
L7        122666 S IC50
L8             0 S L7 (P) L6
L9             6 S L6 (P) (50%) (P) INHIBIT?
L10            2 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11           25 DUPLICATE REMOVE L6 (46 DUPLICATES REMOVED)
L12            1 S L3 (P) L5
L13         2419 S WHITENING AGENT
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L14             1 S IMMUNO? CONTROLLING AGENT
L15             1 S APPETITE CONTROLLING AGENT
L16         25159 S COSMETIC (P) (COMPOSITION OR PREPARATION)
L17         27531 S L13 OR L14 OR L15 OR L16
L18             1 S L17 AND (L6 OR L3)
L19             2 S L17 AND L2
L20             2 DUPLICATE REMOVE L19 (0 DUPLICATES REMOVED)
L21             1 S L20 NOT L18
L22            19 S SHIOJIRI EIJI/AU
L23            14 S TAKINO YOSHINOBU/AU
L24             1 S CHUJOU HIROMI/AU
L25            80 S SAKAMOTO KAZUTAMI/AU
L26             0 S LJICHI CHIORI/AU
L27           119 S ETO YUZURU/AU
L28            68 S IWASAKI KEIJI/AU
L29           271 S L22 OR L23 OR L24 OR L25 OR L27 OR L28
L30             1 S L29 AND (L2 OR L3 OR L6)
L31             0 S L30 NOT L18

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   97.98      98.19

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -1.30      -1.30

STN INTERNATIONAL LOGOFF AT 19:46:49 ON 16 SEP 2003
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